

## **Method of using Unbalanced Alternating Electric Field in Microfluidic devices.**

*Inventors: Andrei S. Dukhin and Stanislav S. Dukhin*

### **Field of the Invention**

This invention describes a method for generating directed relative motion of liquid in micro-fluidic device by applying uniform alternating electric field with “unbalanced” time dependence to the system of the charged micro-obstacles that experience non-linear polarization in the applied electric field, which causes non-linear electro-osmosis.

### **Background of the Invention**

Electric field influence on the charged surfaces generates relative motion of the phases in heterogeneous systems. In the case of “electrophoresis”, particles or macromolecules move relative to the liquid, whereas in the case of “electroosmosis”, liquid moves relative to the solid matrix. These “electrokinetic phenomena” are known for 200 years and are the basis of several important technologies. One of the recent important technological developments exploiting these phenomena is “microfluidics”, which is technology of operating motion of the small volumes of liquid. There is a version of mocofluidic devices that uses electroosmosis as driving force initiating liquid motion. There are several reviews describing current level of microfluidic development: 1. “Microfluidics: Basis Issues, Applications and Challenges”, by H.A. Stone and S.Kim, AIChE Journal, vol. 47, 6, pp.1250-1254, 2001; 2. “Micro Total Analysis Systems. Introduction, Theory and Technology”, by D.R.Reyes, D.Iossifidis, P.A.Auroux, A.Manz, Anal.Chem, 74, 2623-2636, 2002; 3. “Flexible Methods for Microfluidics”, by G.W. Whitesides and A.D. Stroock, Physics Today, 42-48, June 2001.

All devices that employ this effect can be considered as combination of material objects, such as electrodes, canals, valves, etc, and electric field. Accordingly, there are three approaches to achieve specified goals:

- either to arrange material objects at certain appropriate design and order
- or apply electric field with appropriate properties.
- or use both ways together.

US Patent 5,976,336 “Microfluidic devices incorporating improved channel geometries” by R.S.Dubrow, C.B.Kennedy, L.J.Bousse, 1999, might serve as an example of the first approach. In this patent we do not consider material construction of the microfluidic device at all.

In this patent we are dealing exclusively with the second approach.

In the general, electric field strength  $E$  is characterized with frequency  $\omega$ , amplitude  $A$  and phase  $\psi$  as following:

$$E(x, t) = A(x, t) \sin(\omega t + \psi) \quad (1)$$

where  $x$  and  $t$  are some space coordinate and time respectively.

There are two modes of the electric field depending on the frequency:

- DC field at the zero frequency
- AC field at non-zero frequency

The first and most used version is DC field. There are several US Patents dealing with this type of electrokinetic microfluidic devices: by S.J.Salvatore, 4,908,112 “Silicon semiconductor wafer for analyzing micronic biological samples” in 1990; by P.K.Dasgupta, 5,660,703 “Apparatus for capillary electrophoresis having an auxiliary electroosmotic pump” in 1997, by J.W.Parce, 6,394,759 “Micropump” and 6,012,902 “Micropump” in 2000, by Kopf-Sill, 6,617,823 “Systems for monitoring and controlling fluid flows rates in microfluidic systems” in 2003

This mode of the electric field has a big disadvantage of being associated with Faraday current on electrodes. This current is related to electrochemical reactions on electrodes. These reactions generate chemical species, which could cause contamination.

It is possible to prevent, or at least to minimize this contamination managing design of material objects as it is suggested, for instance, by P.K.Dasgupta, 5,660,703 "Apparatus for capillary electrophoresis having an auxiliary electroosmotic pump" in 1997.

Replacing DC field with AC field offers much simpler solution to this problem. In this mode of the electric field, it is possible to eliminate electrochemical reactions completely if frequency is high enough.

However, application of the AC field requires a special means for creating directed motion of the liquid. Just regular linear electroosmosis in symmetrical system does not generate the directed motion of liquid and useless for pumping. This problem could be resolved by introducing asymmetry into the system. This idea is widely known in the generating directed motion of the particles by AC electric field. Non-uniformly spaced AC electric field with the space coordinate  $x$  dependent amplitude generates directed motion of the particles known as "dielectrophoresis". There is a large bulk of literature on dielectrophoresis. One of the most recent patents on this subject is by F.F.Becker, P.R.C.Gascoyne, Y.Huang and X.B.Wang , 6,641,708 "Method and apparatus for fractionation using conventional dielectrophoresis and field flow fractionation", 2003.

The same idea can be introduced for generating directed motion of the liquid. Space dependence of the AC electric field amplitude  $A(x)$  is induced by special arrangements of electrodes. Application of this idea to the microfluidics is described in the several recent papers: by A.Ajdari "Pumping liquids using asymmetric electrode arrays", Physical Review E, vol.61, 1, pp. 45-48, 2000, by A.B.D.Brown, C.G.Smith, and A.R.Rennie "Pumping of water with ac electric fields applied to asymmetric pairs of microelectrodes", Physical Review E, vol.63, 016305, 2000.

This approach to the microfluidic pumping is complicated by the problem of the changing direction of the liquid motion. Asymmetry of the material objects in the device determines this direction. It means that such

devices could pump liquid only in one direction. Voltage modulation suggested by A.Ajdari “Pumping liquids using asymmetric electrode arrays”, Physical Review E, vol.61, 1, pp. 45-48 introduces a constant, time independent component of the current, which constituents return to the DC field with all related problems.

In addition, it might be hard to control asymmetry of the elements on this small scale of dimensions.

In this patent we evoke an old idea expressed many years ago in Russian literature for eliminating linear effects in electrophoresis with purpose of investigating non-linear components of electrophoretic motion. It was suggested by S.S.Dukhin, A.K.Vidybida, A.S.Dukhin and A.A.Serikov “Aperiodic Electrophoresis. Directed drift of dispersed particles in a uniform anharmonic alternating electric field”, Kolloidnyi Zh., vo.49, 5, 752-755, 1988, English.

Instead of the asymmetry of the material object, this idea suggests to use a special time dependence of the electric field, keeping its amplitude uniform, space independent. This type of electric field is called “un-balanced”. It does not have constant, time independent component. This eliminates linear effects, Faraday current, prevents possible contamination by electrochemical reactions residue. At the same time it generates directed motion of the particles, which depends on the non-linear terms in electrophoretic mobility. There is a general definition of this field and some examples given in the detailed description of this patent.

This idea has never been before suggested for electroosmosis and related microfluidic applications.

### **Brief Summary of Invention**

The applicant describes a new method of generating directed motion of the liquid in the microfluidic device by applying “un-balanced” AC electric field for generating electroosmosis and related hydrodynamic flow in the chamber with any symmetry of the elements, including spherical or cylindrical symmetry, and any relative position of these elements. Direction of the flow depends on the phase of the “un-balanced” electric field, which opens a simple way to operate flow and create a desirable flow pattern.

## Brief Description of the Drawings

**Figure 1.** Two examples of the “un-balanced” AC electric field.

## Detailed Description of Invention

Microfluidics is rather new discipline with a purpose of creating new means for operating motion of liquid on very small scales of hundreds microns and below. Microfluidics is closely linked to electrokinetics, which is scientific discipline regarding various phenomena that occur in the heterogeneous systems under influence of electric field. In particular, electrokinetic effect of electroosmosis is of great interest for microfluidics because it could be defined as motion of the liquid generated by the electric field influence on interfacial electric charges.

Electroosmosis is closely related to electrophoresis, which is motion of the solid particles relative to the liquid induced by the external electric field.

These electrokinetic phenomena are known for almost 200 years with most attention paid to electrophoresis in both experimental and theoretical aspects. Some of this knowledge could be transferred and expanded now from electrophoresis to electroosmosis for microfluidics related purposes.

Both effects are characterized with a speed of the motion. In the case of electrophoresis it is motion of particle relative to the liquid  $V_{eph}$ , in the case of electroosmosis it is opposite, motion of liquid relative to the immobile solid phase  $V_{eo}$ . In the imaginary case of the collection of the separate particles in the liquid, speed of electrophoresis is equal to the speed of electroosmosis in magnitude but opposite in sign, because they are simply different due to the difference in the immobile frame of reference.

$$V_{eo} = -V_{eph} \quad (2)$$

In the classical electrokinetic theory (see Dukhin, S.S. and Derjaguin, B.V. “Electrokinetic Phenomena” in “Surface and Colloid Science”, E.Matijevic (Ed.), John Wiley & Sons, NY, v.7 (1974)) electrophoresis and electroosmosis are linear effects in regard to the electric field strength. It happens because

external field electric potential drop associated with a small colloidal particle  $2Ea$  is much less than typical potential in the particles double layers  $RT/F \approx 25 \text{ mV}$ . Here  $a$  is particle radius,  $R$  is a gas constant,  $T$  is absolute temperature,  $F$  is Faraday constant. This usually expressed as the following non-equality:

$$\frac{EFa}{RT} < 1 \quad (3)$$

For particle with 1 micron radius this restrict  $E$  to be below 250 V/cm. The typical value of electric field strength in classical electrokinetics is below 10 V/cm, which explains why electrophoresis and electroosmosis are assumed to be linear with electric field strength. A special notion of “electrophoretic mobility” as coefficient proportionality between speed of electrophoresis and electric field strength has been introduced:

$$V_{eph} = \mu_{eph} E \quad (4)$$

About 2 decades ago it became clear that assumption of linearity does not work in some cases. The notion of “non-linear electrophoresis” was introduce. Review of these earlier works was given by S.S.Dukhin, A.K.Vidybida, A.S.Dukhin and A.A.Serikov “Aperiodic Electrophoresis. Directed drift of dispersed particles in a uniform anharmonic alternating electric field”, Kolloidnyi Zh., vo.49, 5, 752-755, 1988, English. The speed of non-linear electrophoresis contains two terms, classical linear and term proportional to the third power of the electric field strength:

$$V_{eph} = \mu_{eph} E + \mu_{eph,3} E^3 \quad (5)$$

Importance of the non-linear term depends on the value of the non-linear electrophoretic mobility  $\mu_{eph,3}$ . There were theories developed for general non-conducting particles and for two special cases when this parameter is particularly large: 1) porous charged particles such as ionite or polyelectrolyte; 2) metal ideally polarized particles.

For general non-conducting particles (oxides, latex, pigments, etc) non-linear term is related to the polarization of the double layer caused by surface conductivity. There is a dimensionless parameter called “Dukhin number”, (see Lyklema, J., “Fundamentals of Interface and Colloid Science”, vol. 1-3, Academic

Press, London-NY, (1995-2000), which determines the magnitude of this effect. This number is reciprocally proportional to the particle size. In the case of microfluidics the size of obstacles is rather large, certainly exceeding micron. This leads to the small Dukhin number, negligible double layer polarization and small, even hardly measurable non-linear electrophoretic term if obstacles are made from non-conducting material.

For the purpose of this patent the most important is the case of metal particles. Non-linear electrophoresis is the most pronounced in this case. The non-linear term in this case is related to the difference in conductivities between particle and liquid.

Theory of non-linear electrophoresis of metal ideally polarized particles was developed by A.S.Dukhin "Biospecific mechanism of double layer formation and peculiarities of cell electrophoresis", Colloids and Surfaces A, 73, pp.29-48, 1993. He derived the following expression for this effect:

$$V_{eph} = \frac{\varepsilon_m \varepsilon_0 \zeta}{\eta} E - \frac{9\varepsilon_m \varepsilon_0 a^2}{8\eta C_{dl}} \left( \frac{\partial C_{dl}}{\partial \phi} \right)_{\phi=\zeta} E^3 \quad (6)$$

where  $\varepsilon_m$  and  $\varepsilon_0$  are dielectric permittivities of media and vacuum,  $\eta$  is dynamic viscosity,  $\phi$  is electric potential,  $C_{dl}$  is double layer capacitance,  $\zeta$  is electrokinetic potential of particles, which is measure of their equilibrium electric charge.

This simple theory can be directly used for estimating speed of the liquid flow in the microfluidic device with collection of the metal electrodes for generating electroosmotic flow under influence of DC electric field. There is just one difference. Instead of particles moving relatively to the liquid, liquid moves relatively to the fixed cylindrical or spherical electrodes.

$$V_{eo} = -V_{eph} = -\frac{\varepsilon_m \varepsilon_0 \zeta}{\eta} E + \frac{9\varepsilon_m \varepsilon_0 a^2}{8\eta C_{dl}} \left( \frac{\partial C_{dl}}{\partial \phi} \right)_{\phi=\zeta} E^3 \quad (7)$$

This expression allows us to compare linear and non-linear effects. For instance, it turns out that for particle size 10 microns, non-linear term becomes larger than linear term at the electric field strength exceeding only approximately 25 V/cm. In the case of 100 microns particles this critical field is only 2.5 V/cm.

These simple approximate calculations indicate that non-linear electroosmosis could be used as a basis for microfluidic device. It is very fortunate because it opens way to replace DC field with AC field. This replacement is desirable very much because it allows to eliminate Faraday current and related contamination by products of electrochemical reactions.

In order to determine the optimum way to apply AC electric field we again turn our attention to the existing theory of electrophoresis.

Fifteen years ago a group of Ukrainian scientists suggested to use so-called “un-balanced” AC electric field for eliminating linear term in the speed of the particle motion and creating particle drift with the speed that depends only on the non-linear mobility: S.S.Dukhin, A.K.Vidybida, A.S.Dukhin and A.A.Serikov “Aperiodic Electrophoresis. Directed drift of dispersed particles in a uniform anharmonic alternating electric field”, Kolloidnyi Zh., vo.49, 5, 752-755, 1988, English.

The definition of the “un-balanced” electric field could be given in the form of the following two equations:

$$\int_0^T E dt = 0 \quad (8)$$

$$\int_0^T E^3 dt \neq 0 \quad (9)$$

The first equation means that there should be no time independent component of the current in the system. The second one is required for retaining the non-linear term in the particle drifting motion. Figure 1 shows 2 examples of “un-balanced” AC electric field. The top example illustrates the following AC field, which is sum of two harmonics shifted by certain phase:

$$E = E_1 \sin(\omega t) + E_2 \sin(2\omega t + \psi) \quad (10)$$

If we would apply electric field like this to the real dispersion, particle start to drift with the speed that depends on the non-linear mobility only. Consequently, in the case of microfluidic device, liquid would exhibit drifting motion with the following speed:

$$V_{eo}^{drift} = \frac{1}{T_e} \int_0^{T_e} V_{eo} dt = \frac{3}{4} \mu_{ef,3} E_1^2 E_2 \sin \psi = \frac{27}{32} \frac{\epsilon_m \epsilon_0 a^2}{\eta C_{dl}} \left( \frac{\partial C_{dl}}{\partial \phi} \right)_{\phi=\zeta} E_1^2 E_2 \sin \psi \quad (11)$$

where  $T_e$  is the time period of the electric field.

Direction of the motion depends on the phase shift between harmonics. This gives an easy way to operate with liquid motion.

There is infinite number of the various “un-balanced” AC electric fields. We just showed only two examples on the Figure 1. This fields must satisfy conditions (8) and (9) and there is also certain restrictions of the frequency.

First of all, frequency must be above critical frequency of Warburg impedance  $\omega_W$  in order to eliminate Faraday current. It is usually several KHz.

Secondly, frequency must be below Maxwell-Wagner frequency  $\omega_{MW}$  that depends mostly on conductivity of the liquid  $K_m$ , (see Dukhin, S.S. and Shilov V.N. “Dielectric phenomena and the double layer in dispersed systems and polyelectrolytes”, John Wiley and Sons, NY, (1974)):

$$\omega \ll \omega_{MW} = \frac{K_m}{\epsilon_m \epsilon_0} \quad (12)$$

This frequency characterizes relaxation of the double layer. Polarization charges that cause non-linear effect require some time to develop completely. This condition specifies Maxwell-Wagner frequency. For conductivity of liquid  $K_m=0.01$  S/m, this critical frequency equals roughly to 2.2 MHz.

Third condition requires frequency to be below frequency of the electroosmotic field relaxation  $\omega_{eo}$ :

$$\omega \ll \omega_{eo} = \frac{V}{D} \omega_{MW}$$

where  $\nu$  is kinematic viscosity of the liquid,  $D$  is effective diffusion coefficient of the electrolyte.

This condition reflects the fact that electric field should change in time slow enough for allowing electroosmotic flow to develop completely within the double layer. This restriction is not essential in aqueous systems where because kinematic viscosity exceeds diffusion coefficient several order of magnitude. This means that this frequency is much larger than Maxwell-Wagner frequency.

However, there is one more important frequency of hydrodynamic nature. Electroosmotic flow establishes quickly itself within the thin Double Layer. This flow makes liquid to move beyond the double layer. It takes some time for this bulk flow to develop. This critical time depends on the size of the object that generates initial electroosmotic flow. Corresponding frequency of this hydrodynamic relaxation  $\omega_h$  is given as following:

$$\omega \ll \omega_h = \frac{\nu}{a^2}$$

This hydrodynamic relaxation limits available frequency range very substantially in the case of microfluidics. The larger size of the electroosmosis generating obstacles the lower this frequency becomes. For instance, for 100 micron generating electrodes it is only about 0.1 KHz. This means that for large microfluidic device obstacles of hundreds microns in size, it is practically impossible to take advantage of all benefits related with AC field. Hydrodynamic flow would not have sufficient time to develop completely if frequency high is enough to eliminate Faraday current.

It looks like the size of the electroosmosis generating obstacles should not exceed 10 microns. Hydrodynamic relaxation frequency corresponding to this size is about 10 KHz. This opens the frequency window between Warburg frequency  $\omega_W$  (several KHz) and hydrodynamic relaxation frequency  $\omega_h$  (about 10 KHz).